Interdisciplinary headache care in Switzerland

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Interdisciplinary Headache Care in Switzerland

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PREAMBLE

It was during the 4th year's teaching course, given by *Dr. Reto Agosti* at the University of Zurich, when I discovered my interest for neurology, and especially headaches. So I started my doctoral thesis at the Headache and Pain Clinic (HPC) at the Department of Neurology. I not only had the opportunity to collect and analyze data of a few hundreds of headache patients, but also to benefit from the experience of the founder of the HPC and first president of the Swiss Headache Society, *Dr. Hansruedi Isler*. It was then a great success for me as a student, when I won an award for the best poster at the World Headache Conference in London in 2000. This was furthermore highly stimulating to continue a career combining clinical work and research.

Due to my mentor and greatly appreciated colleague *PD Dr. Peter Sándor*, who introduced me to *Prof. Peter Goadsby* and *Dr. Holger Kaube*, I started as a research fellow at the Headache Group, Institute of Neurology, Queen Square in London, shortly after I passed my state examination. In the following two years I had the great possibility to learn clinical skills from two headache experts, and to benefit from a melting pot of rare headache syndromes at the National Hospital for Neurology and Neurosurgery. Research-wise we started an electrophysiological project to gain more insights into migraine pathophysiology. We used photic stimulation techniques and evoked potential recording to investigate the early phase of migraine in comparison to healthy volunteers.

Back in Switzerland I started my clinical training in neurology, where I also had to experience the difficulties of combining clinical duties, family life, and research. After 3 years of basic training at RehaClinic Bad Zurzach and at the Cantonal Hospital Aarau, I continued at the department of Neurology, University Hospital Zurich. In May 2010 I was appointed to lead the HPC, as an 'Oberarzt'. In this quite small research team of only 3 to 5 collaborators, our group published more than 20 peer-reviewed publications in the field of headaches from 2008 onwards (12 with own contribution).

Since July 2012 I've been working as a 'Leitender Arzt' at the Neurorehabilitation Center RehaClinic Bad Zurzach, where we also provide an inpatient program for medication overuse headache, chronic migraine, and posttraumatic headaches. I am still collaborating with colleagues from the University Hospital Zurich (Headache and Pain Clinic at the Department of Neurology (lead *PD Dr. A. Palla*); Department of Neurosurgery; Ambulatory Pain Clinic; and Division of Cranio-Maxillo-Facial and Oral Surgery) to provide access to neuromodulation for patients with chronic and treatment-refractory headaches.

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SUMMARY

Headaches are not only among the top causes why patients seek help from doctors; they also have a high socio-economic impact. The International Headache Society has classified more than 250 different headache types, whereof tension type headache and migraine account for the most frequent ones. While many patients never see a doctor because of their headaches, and numerous are treated in primary care, some patients need help from a headache specialist and will be referred to a headache center. They might suffer from a rare type of headache, the headache might have deteriorated, or it might be refractory to treatment.

The Headache and Pain Clinic (HPC, Kopfwehsprechstunde) was founded at the Department of Neurology, University Hospital Zurich in 1966. Since then it remained a tertiary care center for the assessment and management of difficult to treat headache problems, which often requires multimodality and interdisciplinarity. Since its foundation it was also a main goal to improve collaboration with primary care. In ***study A*** we described the characteristics of the population of headache patients at the HPC. Most patients were diagnosed with migraine or a combination of migraine and tension type headaches. The coexistence of migraine and tension type headache, as well as the high frequency of headache days would have excluded most migraine patients from typical drug trials: at best, only one third of the tertiary care population would be eligible. This demonstrates some limits of evidence-based medicine for a subpopulation of highly affected patients.

In ***study B*** we compared two samples of patients from primary and tertiary care. The differences in management strategies mainly reflected differences in headache severity and chronicity. The shortcomings of diagnosis and treatment in primary care seemed to be minimized by the involvement in such an investigation. The awareness of headache in primary care was the focus of ***study C***. In cooperation with the Swiss Headache Society we conducted a survey about the frequency of headache patients in GP practices and inquired about their treatment and referral strategies. General practitioners provide first access for most undiagnosed headache patients. Therefore efficient and correct diagnosis and management is eminent, especially when patients have to be referred for further evaluation. Both patients and physicians may benefit from a well-functioning 'bidisciplinary' cooperation.

As an advantage, a tertiary headache centers may function like a melting pot for rare headaches disorders. For instance, the largest series of SUNCT, a rare neuralgiform

autonomic headache, comes from the Headache Group, Institute of Neurology, Queen Square in London, UK. In ***study D*** we describe a series of patients with orofacial cluster headache, a form of cluster headache with an atypical localization, which is usually first seen in the dental practice. Thus, the series was published in cooperation with colleagues from the dental hospital, University Zurich. In ***study E*** we described adults with acute confusional migraine, again in cooperation with colleagues from other headache centers and from secondary care. Acute confusional migraine is most probably a subtype of migraine with aura which can typically be seen in children and adolescents. In adults the differential diagnosis to more hazardous diseases, like stroke or epilepsy, may be challenging.

Finally, a headache center is not only a predisposed partner for randomized-controlled multicenter trials, there is also room for clinical field-testing or even development of new treatment options in a multidisciplinary setting. In ***study F*** we described the largest series of steroid injections of the greater occipital nerve for the treatment of acute and chronic cluster headache. We were able to show that infiltration of the greater occipital nerve is a valuable and safe option in the clinical setting. In cooperation with the Department of Women's Health we published retrospective data of 38 women with migraine (***study G***), who used a progestin-only pill for contraception. In these patients, migraine tended to improve in frequency and intensity.

The present work highlights the elements of interdisciplinary headache care at the tertiary level: a good collaboration of all the different partners and specialists, keeping up-to-date with the latest treatment developments, and foremost being close to the patient.

Publications included in the cumulative habilitation

A. Kozak S, Gantenbein AR (*equally contributed*), Isler H, Merikangas KR, Angst J, Gamma A & Agosti R. Nosology and treatment of primary headache in a Swiss Headache clinic. Journal of Headache & Pain 2005; 6(3):121-7.

B. Gantenbein AR, Kozak S, Agosti F, Agosti R & Isler H. Headache patients in primary care and a tertiary care unit in Zürich, Switzerland. Cephalalgia 2006; 26(11):1451-7.

C. Gantenbein AR, Jäggi C, Sturzenegger M, Gobbi C, Merki-Feld GS, Emmenegger MJ, Taub E, Sándor PS. Awareness of headache and of national headache society activities among primary care physicians - a qualitative study. BMC Res Notes 2013; 6(1):118.

D. Gaul C, Gantenbein AR (*equally contributed*), Buettner UW, Ettlin DA & Sándor PS. Orofacial cluster headache. Cephalalgia 2008; 28(8):903-5.

E. Gantenbein AR, Riederer F, Mathys J, Biethahn S, Gudrun Gossrau G, Waldvogel D & Sándor PS. Confusional migraine is an adult as well as a childhood disease. Cephalalgia 2011; 31(2):206-12.

F. Gantenbein AR, Lutz NJ, Riederer F & Sándor PS. Efficacy and safety of 121 injections of the greater occipital nerve in episodic and chronic cluster headache. Cephalalgia 2012; 32:630-4.

G. Merki-Feld GS, Imthurn B, Seifert B, Langner R, Sándor PS & Gantenbein AR. Headache frequency and intensity in female migraineurs using desogestrel-only contraception: a retrospective pilot diary study. Cephalalgia 2013; 33(5):340-6.

INTRODUCTION

In 1988 the International Headache Society has defined criteria for classification of headache disorders for the first time [1]. These criteria have been revised in 2004 [2] and the 3rd edition is expected in mid-2013. There are criteria for more than 250 headache disorders, whereof tension type headache, migraine and cluster headache account for the most frequent of all primary headaches. While tension type headaches do in general not interfere with daily activity, migraine may often be very disabling [3], and cluster headache even belongs to the most severe pain disorders. In 2001 the World Health Report ranked migraine among the 20 diseases with most years of life lived with disability [4]. Several studies of the last decades have highlighted the socio-economic impact of migraine (for a review see [5]).

In a recent publication the European Headache Federation assessed the needs and demands for headache care and made a proposal for the organization of headache service in Europe [6]. Three different levels are described, primary care, special-interest care and headache centers, with an advanced multidisciplinary setting. It is self-evident that most headache patients are being treated in primary care. However, for difficult-to-treat headache disorders and rare headache types, secondary, but also tertiary headache care providers are important. The Headache and Pain Clinic (Kopfwehsprechstunde) at the Department of Neurology at University Hospital Zurich, was established in 1966. Since then it remained a service for the assessment and management of difficult headache problems. Patients usually are referred by general practitioners and specialists. Most patients have been treated unsuccessfully by several physicians and laymen before. They often require time-consuming and individualized care, in a multimodal and interdisciplinary setting.

In this cumulative habilitation I will describe the Headache and Pain Clinic at the University Hospital of Zurich [A,B]. I will demonstrate the value of a good cooperation with general practice [B,C]. Furthermore I will highlight the benefits of a tertiary headache center in respect of generating clinical implications by two examples of rare headache disorders [D,E] and the development and clinical testing of new treatments options [7-9,F,G]. By those means I want to provide strong arguments for the importance of interdisciplinary and headache care at tertiary level.

ABSTRACTS OF INCLUDED PUBLICATIONS

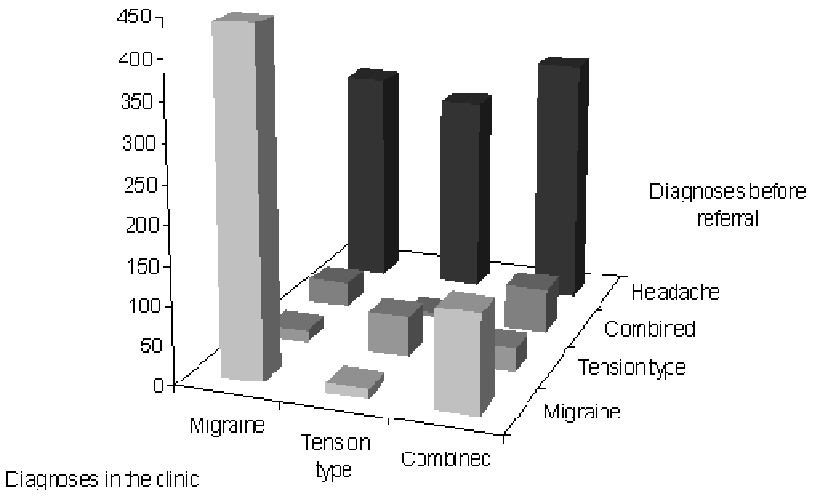
Study A: Nosology and treatment of primary headache in a Swiss Headache clinic.

Methods. Retrospective description of all patients with migraine, tension type headache and combinations of migraine and tension type headache who were seen at the headache and pain clinic, Department of Neurology, University Hospital Zurich, in the years 1996 to 1998 (n=1625). Demographical and clinical data, drugs, physical and alternative treatments before and after referral were collected. Descriptive statistics were used for differences between the sample, headache subtypes and the general population.

Results. According to the IHS criteria the patients were diagnosed with migraine in 47.3%, with tension type headaches in 20%, and in 32.7% with a combination of both (see also figure 1). On average migraine patients had a lower frequency of headache days per month than tension type headache patients. The most frequent special investigations were: CT scan (18.2% before, 7.6% after first consultation), EEG (10% before, 2.3% after first consultation) and MRI (5.5% before, 3.8% after first consultation). No pathology was found which would have led to further interventions. The most frequently reported complementary treatments were acupuncture (n=338) and homeopathy (n=120), while all other methods were reported by small minorities.

Conclusion. The coexistence of migraine and tension type headache, and the high frequencies of headache days would have excluded most migraine patients from typical drug trials: at best, only one third were eligible. The socioeconomic impact of combined and difficult headache syndromes calls for comprehensive management.

Figure 1. More than one half of the migraine patients was referred as migraine but only one sixth of the tension type headaches, and one tenth of the combined headaches came in with a correct diagnosis. Most of the headaches have been referred as “unspecific headache”.



Study B: Headache patients in primary care and a tertiary care unit in Zürich, Switzerland.

Methods. Demographic features, severity of disorders, and medical management were compared between primary and tertiary care. Case-control study with data from 181 randomly selected patients at the headache and pain clinic (HPC), Department of Neurology, University Hospital Zurich, and 181 patients from 20 general practitioners (GP) from the region of Zurich.

Results. There was a predominance of women and socially underprivileged individuals in both samples. Chronic headache was overrepresented in the HPC (44.7%). Loss of work above two months was found exclusively in the HPC (9.9%). In the GP sample 89.5% were using attack treatment, and 59.7% were treated with prophylactics. In the HPC 90.6% took acute drungs and 67.4% were on a preventive. One third of both groups had had complementary and alternative medical treatment.

Conclusion. Differences in management strategies reflected differences in headache severity and chronicity. Results indicated that remaining shortcomings of diagnosis and treatment of headache in primary care could be minimized by involving GPs in similar non-commercial studies.

Study C: Awareness of Headache and of National Headache Society Activities among Primary Care Physicians - a qualitative study.

Methods. In a qualitative telephone survey, targeting primary care practices, we asked about the frequency of headache patients in their practices and inquired about their treatment and referral strategies.

Results. A total of 1000 telephone interviews with primary care practices were conducted. Three-hundred and fifty physicians were directly interviewed, 95% of them see headache patients every week, 23% daily. Direct MRI referral was done by 84%. Sixty-two per cent of the physicians knew the Swiss headache society, 73% were interested in further education about headaches.

Conclusion. The survey yielded information about the physicians' awareness of the Swiss Headache Society and its activities, and about their desire for continuing education in the area of headache. National headache societies should work to improve the cooperation between headache specialists and PCP, aiming for a better care for patients with headache.

Study D: Orofacial cluster headache.

Methods. Case series of patients who fulfill diagnostic criteria for cluster headache, but experience excruciating pain - rather than headache - in the distribution of the 2nd or 3rd trigeminal divisions.

Conclusion. Lacking a diagnostic concept, these patients tend to receive inadequate medical and dental treatment, including multiple tooth extractions. We review similar cases in the literature and discuss a possible extension of the localisation criteria for cluster headache.

Study E: Confusional migraine is an adult as well as a childhood disease.

Methods. Acute confusional migraine is considered a rare migraine variant primarily seen in children and adolescents. Case series of eight adults and two adolescents suffering from migraine attacks associated with transient confusional states.

Results. Eight patients reported two or more such attacks. One of them reported mild head trauma in the past. One patient reported mild head trauma as a possible trigger. Further investigations were unremarkable in all patients and did not suggest underlying structural abnormalities.

Conclusion. Our findings propose expanding the concept of confusional migraine from the pediatric population to adults. The temporal course of the confusion as well as the association with visual and other aura symptoms suggest cortical spreading depression as the underlying pathophysiology.

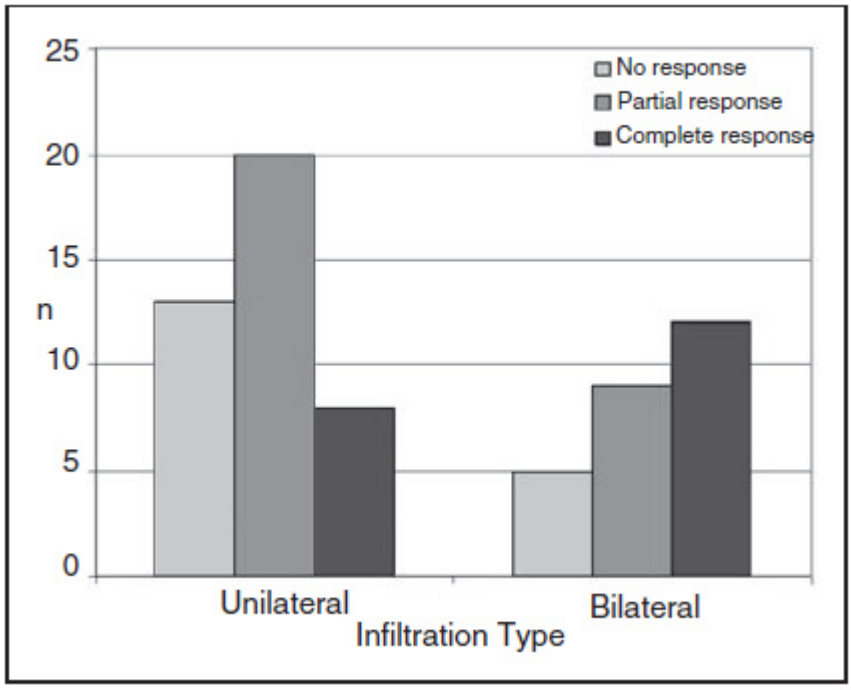
Study F: Efficacy and safety of 121 injections of the greater occipital nerve (GON) in episodic and chronic cluster headache.

Methods. Retrospective analysis of efficacy and safety of 121 injections of the greater occipital nerve in 60 consecutive patients with episodic or chronic cluster headache, over a period of 4 years.

Results. Almost 80% of the infiltrations were at least partially effective (reduction of attack frequency, duration or severity) and 45% resulted in a complete response (no further attacks). The effect was maintained for a median of 14 days in chronic cluster headache, and 25 days in episodic cluster headache. In 18 infiltrations (=14.2%), transient side effects were reported, such as local pain, steroid effects, or syncope.

Conclusion. The data show that infiltration of the greater occipital nerve is a valuable and safe option in the clinical setting to treat patients suffering from cluster headache, especially for the episodic form.

Figure 2. Bilateral versus unilateral infiltrations in patients with chronic cluster headache, indicating better response rates for bilateral injections.



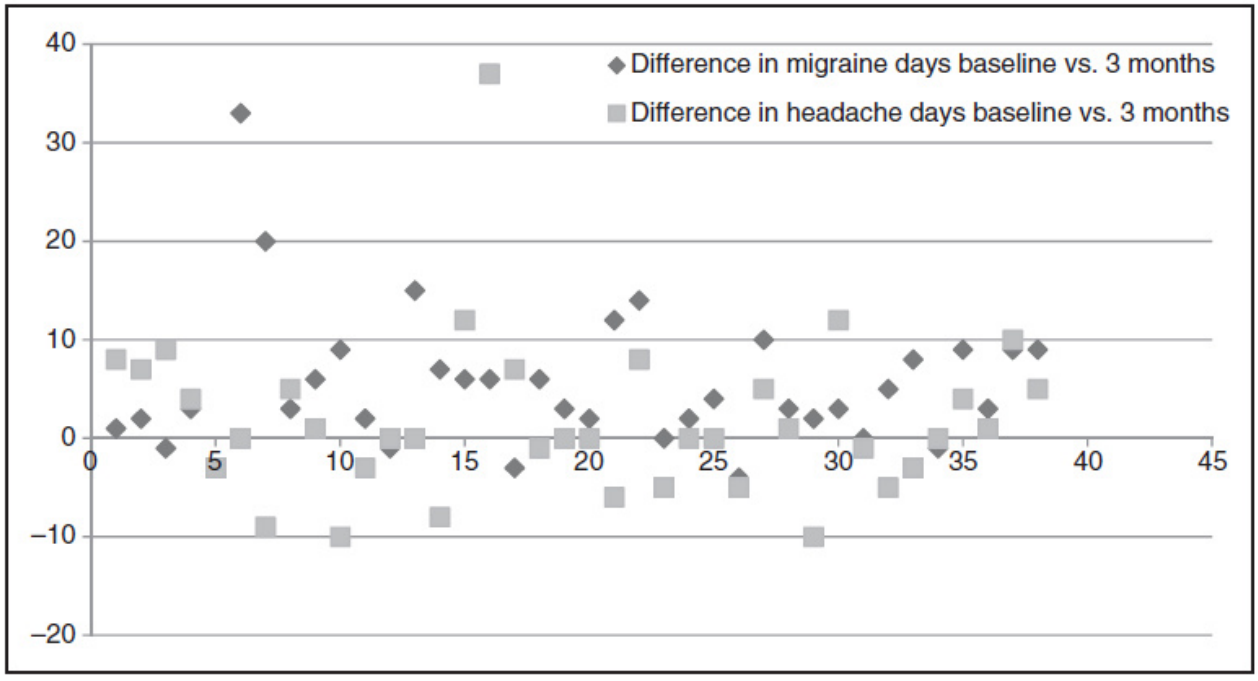
Study G: Headache frequency and intensity in female migraineurs using desogestrel-only contraception: A retrospective pilot diary study.

Methods. A retrospective diary study of women with migraine, who used desogestrel 75µg as an oral contraceptive. Out of 58 women, 38 had completed headache diaries for a period of 6 months. Incomplete diaries (n=12), side effects (n=5), and loss to follow-up (n=3), were the reasons for the exclusion of 20 subjects. The 90 days before (baseline) and after (on oral contraception) initiation of the progestin were compared.

Results. Days with migraine, days with all kind of headache, and days with use of any headache medication, were significantly reduced at follow-up after three months. In addition there was a reduction in headache intensity ($p<0.0001$). The reduction in number of days with use of triptans was not significant ($p<0.14$).

Conclusion. Our data indicate that the progestin-only pill desogestrel 75µg in addition to providing efficient contraception tends to improve migraine frequency and intensity in female migraineurs. Because of the limitations of our study with regard to sample size and design as an observational investigation, these results are at too early a stage to draw definite conclusions.

Figure 3. Individual patient data for absolute change in migraine and headache days after 90 days of treatment with desogestrel 75 µg.



COMMENTARY

In ***study A*** we described the characteristics of the Headache and Pain Clinic (Kopfwehsprechstunde), a typical tertiary headache care unit. We know that difficult-to-treat headache problems may cumulate in such centers. However, there are only a few studies describing the population of headache patients in tertiary care. In contrary to the general population, where tension type headache is the most prevalent headache type [10], most patients in tertiary care suffer from migraine [11,12]. The coexistence of migraine and tension type headache, as well as the high frequency of headache days would have excluded most migraine patients from typical drug trials [13]: at best, only one third of the tertiary care population would be eligible. This is an additional demonstration of the complexity of tertiary headache care, and depicts some limitations of evidence-based medicine, as there is almost no evidence for how to treat rare or complex medical problems [14]. Two further publications with own contribution may support this statement, potential treatment options for orgasmic headache [15], or episodic cluster headache [16]. On the whole, multidisciplinary headache management becomes crucial [17].

In ***study B*** we compared a sample of patients from tertiary care with patients in general practice. Most differences were explained by differences in headache severity and chronicity. However, the results also indicated that remaining shortcomings of diagnosis [18,19] and treatment of headache in primary care could be minimized by involving GPs in such non-commercial studies. Only recently, the International Headache Society initiated a Primary Care Interest Group for the improvement of the clinical management of migraine and headache [20]. The same author encouraged research into headache in primary care [20]. In a pioneer survey of the Swiss Headache Society we were investigating the awareness of headache among general practitioners. As ***study C*** shows, almost ¼ of the general practitioners see headache patients every day. More than sixty per cent knew the Swiss headache society, and almost ¾ were interested in education about headaches. A large percentage of primary care physicians directly ordered MRI scans. This was an unexpected finding, with possible implications for health-care costs. In the older study [B] the number was smaller. However, a recent study from the U.K. concluded that GPs who know the correct indications for MRI may appropriately select patients with headaches for neuroimaging [21], even with potential financial savings.

As discussed above, there is not only an accumulation of complex, but also of rare headache disorders in tertiary headache centers. The largest series of SUNCT, a rare

neuralgiform autonomic headache, comes from the Headache Group, Institute of Neurology, Queen Square London, UK [22]. Also the first published familial SUNCT-syndrome was from the outpatient clinic at Queen Square [23]. In ***study D*** we described a case series of orofacial cluster headache. This form of cluster headache presents with pain in the second or third trigeminal branch, and is typically first seen in the dental practice. From the collaboration with the colleagues from the dental hospital, University Zurich, there is another series with atypical presentation of migraine pain [24]. In ***study E*** we described a series of adults with acute confusional migraine. Most probably a subtype of migraine with aura, it is well known in children and adolescents [25,26]. Thus, when presenting in adults the differential diagnosis to hazardous diseases, like stroke or epilepsy, may be more difficult.

Most multicenter randomized-controlled trials are conducted at large tertiary headache centers. The HPC was involved in some pivotal studies [7-9]. ***Publications F & G*** are two examples of uncontrolled studies with direct clinical implications. ***Study F*** is the largest series of steroid injections of the greater occipital nerve for the treatment of acute and chronic cluster headache. A French group published a randomized controlled trial with 43 subjects using a slightly different protocol, supporting that suboccipital nerve blocks are a valuable and safe option in the treatment of cluster headache [27]. ***Study G*** is a retrospective pilot study of 38 women with migraine with and without aura, who used a progestin-only pill for contraception. While migraine seems substantially related to hormonal changes, not only migraine, but also the use of combined oral contraceptives, are associated with an increased risk for vascular events [28]. Therefore progestagen-only contraception is an alternative, which was first studied by an Italian group in migraine with aura [29]. Their pilot study showed a reduction of migraine attacks and of the duration of visual auras. In our sample also women with migraine without aura had a benefit from the estrogen-free contraception.

All the presented work highlights the elements of interdisciplinary headache care at the tertiary level. A good collaboration of all the different partners and specialists, keeping up-to-date with the latest treatment developments, and foremost being close to the patient, should be the main goals.

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Appendix: FULL PUBLICATIONS